
Amendment to the Claims

The Examiner indicated that the claims were in condition for allowance, pending cancellation of unelected inventions. Claims 96-107 and 109-110 (drawn to invention Group II), claim 108 (drawn to invention Group V), and claims 112-115 (drawn to invention Group VI) are cancelled herein, as drawn to non-elected inventions, without prejudice to subsequent renewal. Claim 73 is amended herein solely to cancel non-elected substitutions as dictated by the restriction requirement made final. Please note that Applicants reserve the right to file subsequent applications claiming the canceled subject matter, and that the claim amendments and cancellations should not be construed as abandonment of any presently or previously claimed subject matter or agreement with any objection or rejection of record.

By way of this amendment, claims 73-95 and 111 are pending in the application.

Restriction Requirement

In response to the Restriction Requirement, Applicants had elected Group I, claims 73-95, for prosecution in this application. The Examiner subsequently rejoined Group I (claims 73-95) with Group III (claim 111), and made final a restriction of claim 73 between the substitutions Q49N+Q51S/T and F111N+R113S/T. Applicants confirm election of the substitutions Q49N+Q51S/T.

Drawings

The Examiner has indicated the drawings have been approved by the draftsperson.

Information Disclosure Statements

Under separate cover (via hand-delivery to the Examiner), Applicants are re-submitting the IDS Form PTO-1449 and the 40 references (denoted AA-BN) cited therein which were originally submitted to the USPTO on June 25, 2001. Although Applicants have received a date-stamped return receipt postard showing the IDS and the 40 cited references were received

by the USPTO/OIPE on June 28, 2001, the Examiner has indicated the IDS and cited references cannot be located.

Under the same cover, Applicants are also submitting a Supplemental IDS Form PTO-1449 and 11 references (numbered 1-10) cited therein.

Applicants wish to point out an inadvertent typographical error which led to an incorrect reference being cited in the IDS Form-1449 originally submitted June 25, 2001. Reference "AZ", EP 539 300, was actually meant to be EP 529 300. Provided in the Supplemental IDS is the intended reference EP 529 300 B1, plus an English translation thereof. Applicants are also providing in the Supplemental IDS the Derwent Abstracts (in English) for the two foreign-language documents cited in the IDS Form-1449 originally submitted June 25, 2001: for the mistakenly-provided EP 539 300 (Reference "AZ" as described above) and for WO 98/48018 (Reference "AN").

Applicants respectfully request the information cited in the above-noted Forms PTO-1449 be expressly considered by the Examiner during prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Substitute Sequence Listing

Also under separate cover (via hand-delivery to the Examiner), Applicants are providing a substitute Sequence Listing in paper and CRF diskette format, to which the peptide tag sequences shown on page 41 (SEQ ID NOs:39-45) have been added and bibliographic information has been updated, to comply with the requirements of 37 C.F.R. §1.821.

CONCLUSION

In view of the forgoing, Applicants believe that all formal matters have been addressed and all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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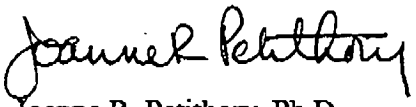
If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 298-5452.

Respectfully submitted,



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APPENDIX A

"MARKED UP" CLAIMS ILLUSTRATING THE AMENDMENTS MADE TO THE CLAIMS OF 09/648,569 WITH ENTRY OF THIS AMENDMENT

insertions indicated by double underlining, deletions indicated by ~~strikethrough~~

73. (Amended) An interferon β polypeptide variant exhibiting an interferon β activity, comprising a variant sequence which differs from the wildtype human interferon β sequence SEQ ID NO:2 in no more than 15 amino acid residues and which comprises ~~one or~~ the substitutions Q49N+Q51S/T relative to SEQ ID NO:2, ~~selected from the group consisting of:~~

~~(a) Q49N+Q51S/T; and (b) F111N+R113S/T.~~

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APPENDIX B

CLAIMS PENDING IN USSN 09/648,569 WITH ENTRY OF THIS AMENDMENT

73. (Amended) An interferon β polypeptide variant exhibiting an interferon β activity, comprising a variant sequence which differs from the wildtype human interferon β sequence SEQ ID NO:2 in no more than 15 amino acid residues and which comprises the substitutions Q49N+Q51S/T relative to SEQ ID NO:2.

74. The variant of claim 73, wherein the variant sequence comprises the substitutions Q49N, Q51T, F111N, and R113T.

75. The variant of claim 73, wherein the variant sequence further comprises at least one substitution relative to SEQ ID NO:2 selected from: K19R; K33R; and K45R.

76. The variant of claim 75, wherein the variant sequence comprises the substitutions K19R, K33R, K45R, Q49N, Q51T, F111N, and R113T.

77. The variant of claim 73, wherein the variant sequence further comprises at least one substitution at a position relative to SEQ ID NO:2 selected from: M1; C17; N80; and V101.

78. The variant of claim 77, wherein the variant sequence comprises the substitutions C17S, Q49N, Q51T, F111N, and R113T.

79. The variant of claim 73, wherein the variant sequence differs from SEQ ID NO:2 in no more than 12 amino acid residues.

80. The variant of claim 79, wherein the variant sequence differs from SEQ ID NO:2 in no more than 10 amino acid residues.

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81. A polypeptide conjugate exhibiting interferon β activity, which conjugate comprises

(a) the variant of claim 73, and

(b) at least one non-polypeptide moiety covalently attached to the variant.

82. The conjugate of claim 81, wherein the non-polypeptide moiety is selected from: a polymer molecule, a sugar moiety, a lipophilic compound, and an organic derivatizing agent.

83. The conjugate of claim 81, wherein the non-polypeptide moiety and the variant are directly covalently joined to one another, or are indirectly covalently joined to one another.

84. The conjugate of claim 82, comprising at least one sugar moiety or at least one polymer molecule covalently attached to the variant.

85. The conjugate of claim 84, comprising at least one sugar moiety and at least one polymer molecule covalently attached to the variant.

86. The conjugate of claim 85, wherein the variant sequence comprises the substitutions Q49N, Q51T, F111N, and R113T.

87. The conjugate of claim 81, wherein the variant sequence further comprises at least one substitution relative to SEQ ID NO:2 selected from: K19R; K33R; and K45R.

88. The conjugate of claim 87, wherein the variant sequence comprises the substitutions K19R, K33R, K45R, Q49N, Q51T, F111N, and R113T.

89. The conjugate of claim 81, wherein the variant sequence further comprises at least one substitution in a position relative to SEQ ID NO:2 selected from: M1; C17; N80; and V101.

90. The conjugate of claim 89, wherein the variant sequence comprises the substitutions C17S, Q49N, Q51T, F111N, and R113T.

91. The conjugate of claim 84, wherein the sugar moiety is covalently attached to an asparagine residue of the variant.

92. The conjugate of claim 91, wherein the sugar moiety is covalently attached to an asparagine residue of the variant selected from the group consisting Q49N, N80, and F111N.

93. The conjugate of claim 84, wherein the polymer molecule is covalently attached to a lysine residue of the variant.

94. The conjugate of claim 84, wherein the polymer molecule is covalently attached to the N-terminus of the variant.

95. The conjugate of claim 84, wherein the polymer molecule comprises a linear polyethylene glycol or a branched polyethylene glycol.

111. A composition comprising the variant of claim 73 or the conjugate of claim 81 and a pharmaceutically acceptable diluent, carrier, excipient or adjuvant.

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APPENDIX C

"MARKED UP" PARAGRAPHS ILLUSTRATING THE AMENDMENTS MADE TO THE SPECIFICATION OF 09/648,569 WITH ENTRY OF THIS AMENDMENT

insertions indicated by double underlining, deletions indicated by ~~strikethrough~~

A. The paragraph at page 2, lines 21-22:

Interferon β molecules with a particular glycosylation pattern and methods for their preparation have been reported (EP 287075 and EP 5329300).

B. The paragraphs at page 41, lines 20-33:

The identity of the specific tag to be used is not critical as long as the tag is capable of being expressed with the polypeptide and is capable of being immobilised on a suitable surface or carrier material. A number of suitable tags are commercially available, e.g. from Unizyme Laboratories, Denmark. For instance, the tag may be any of the following sequences:
His-His-His-His-His-His (SEQ ID NO:39)
Met-Lys-His-His-His-His-His-His (SEQ ID NO:40)
Met-Lys-His-His-Ala-His-His-Gln-His-His (SEQ ID NO:41)
Met-Lys-His-Gln-His-Gln-His-Gln-His-Gln-His-Gln-His-Gln (SEQ ID NO:42)
(vectors useful for providing such tags are available from Unizyme Laboratories, Denmark)
or any of the following:
EQKLI SEEDL (a C-terminal tag described in Mol. Cell. Biol. 5:3610-16, 1985; SEQ ID NO:43)
DYKDDDDK (a C- or N-terminal tag; SEQ ID NO:44)
YPYDVPDYA (SEQ ID NO:45)

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